

Applicant earnestly solicits early and favorable action by the Examiner on this application. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is respectfully urged to telephone the undersigned at 212-801-2146. The undersigned may also be contacted via e-mail at rzucidloe@gtlaw.com.

AUTHORIZATION

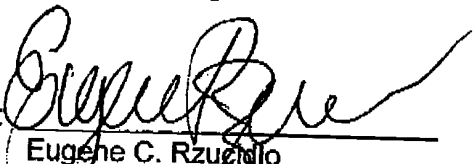
The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 50-1561.

Respectfully submitted,

Greenberg Traurig LLP

Date: December 11, 2002

By:


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20. (Amended) A food supplement for restoring compromised reproductive function comprising a food and an aqueous and/or alcohol extract of *Withania somnifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides.

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Please add new claims 31-46 as follows:

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31. (New) The composition of claim 16, wherein the extract is an aqueous extract.
32. (New) The composition of claim 16, wherein the extract is an alcohol extract.
33. (New) The composition of claim 32, wherein the alcohol is ethanol.
34. (New) The composition of claim 16, wherein the reproductive function is sperm count in a male subject.
35. (New) The composition of claim 34, wherein the extract is an aqueous extract.
36. (New) The composition of claim 34, wherein the extract is an alcohol extract.
37. (New) The composition of claim 36, wherein the alcohol is ethanol.
38. (New) The food supplement of claim 20, wherein the extract is an aqueous extract.
39. (New) The food supplement of claim 20, wherein the extract is an alcohol extract.
40. (New) The food supplement of claim 39, wherein the alcohol is ethanol.
41. (New) The composition of claim 20, wherein the reproductive function is sperm count in a male subject.
42. The food supplement of claim 41, wherein the extract is an aqueous extract.

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43. The food supplement of claim 41, wherein the extract is an alcohol extract.
44. The food supplement of claim 43, wherein the alcohol is ethanol.
45. (New) A method of restoring male reproductive function compromised by an endocrine disturbing chemical comprising administering an effective amount of an alcohol and/or aqueous extract of a root, leaf or whole plant of Withania somnifera Dunal to a male subject in need of such treatment, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides.
46. (New) The method of claim 45, wherein the male reproductive function is sperm count of a male subject.

Restriction Requirement

The Examiner required restriction under 35 U.S.C. §121 to one of the following inventions: Group I, claims 15, 17, 19, 23, 24, 27, and 28 drawn to a composition comprising *Withania somnifera* and a method for restoring compromised reproductive function with said composition, and Group II claims 16, 18, 20, 21, 22, 29 and 30 drawn to a composition comprising an extract of *Withania somnifera* and a method for restoring compromised reproductive function with said composition.

In the Office Action of September 10, 2002, the Examiner noted that a provisional election was made with traverse to prosecute the invention of Group II, claims 16, 18, 20, 21, 22, 29 and 30 during a telephone conversation with Eugene Rzucidlo on 8/15/02 and requested that applicants affirm the provisional election with traverse to continue prosecution for the invention of Group II. Applicants hereby comply with the Examiners' request and elect the invention of Group II, claims 16, 18, 20, 21, 22, 29 and 30, with traverse.

Applicants believe that there is no substantial difference between the effects of the plant and its extract on compromised reproductive function. Both the plant itself, which contains various ingredients, and the extracted ingredients when administered to a human subject in need of such treatment can make

compromised reproductive function recover. For this reason, applicants urge reconsideration and withdrawal of the restriction requirement. The Examiner is further requested to examine all groups in one application.

New claims 31-46 likewise claim compositions and methods for restoring male reproductive function compromised by an endocrine disturbing chemical with an alcohol and/or water extract of *Withania somnifera* wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides. These new claims therefore are included within elected Group II.

35 U.S.C. §112 rejection

The Examiner rejected claims 16, 18, 20, 21, 22, 29, and 30 on the ground that the specification did not enable a person of skill in the art, to make and use a composition/method comprising any extract of *W. somnifera* for restoring compromised reproductive function because that would require undue experimentation.

The Examiner alleged that the term "extract" in the claims is so broad as to render the claims unpredictable, i.e., because any purification of any product to yield a specific phytochemical would constitute an "extract," a skilled artisan would have to ascertain what other extracts besides aqueous and alcoholic extracts of *W. somnifera* would increase sperm count and which, if any extract, would actually increase reproductive function. The Examiner alleged that this would involve tedious trial and error protocols without the expectation of success.

The Examiner further alleged that applicants have not demonstrated wherein other extracts, such as the pressed juice or an organic solvent extract, would provide for similar effects, have not provided extraction protocols or procedures to quantitatively determine phytochemical constituents present in samples obtained from extraction procedures, and have not provided evidence to support the efficacy of such extracts. The Examiner further alleged that unpredictability with regard to plant extracts is documented in the art, and cited

Revilla, et al., J. Agric. Food Chem. 46: 4592-97 (1998) as showing that the slightest variations in polarity of solvent and reaction time upon grape extraction provided respective products with unique characteristic properties; each product in turn would possess varying pharmacological properties based upon their respective phytochemical constituents.

The Examiner further alleged that the claims are not enabled for "restoring reproductive function" because the data concerning the viability and reproductive nature of the sperm is unconvincing. First, the Examiner alleged that there is no substantial difference in the motile sperm rate data in table 6. Second, the Examiner alleged that no nexus has been established, either in this application or in the prior art, between *W. sominifera*'s ability to increase sperm count and any benefits with regard to the etiology of reproduction. Third, the Examiner alleged that although *W. sominifera* may increase sperm count, the viability and reproductive nature of the sperm is highly questionable based on data in this application and data in L. C. Garg and G.C. Parasar, Planta Medica 13: 46-47 (1995), which showed that mice fed *W. sominifera* had decreased litter size and even increased infertility rate. (Table 1, p. 47).

The Examiner further alleged that claims drawn to pharmaceutically acceptable compositions and to methods of administering compounds to humans generally require supporting evidence because of the unpredictability in biological responses to therapeutic treatments.

An enablement rejection can be overcome by demonstrating, by argument and/or evidence, that at the time of filing, a skilled artisan would be able to make and use the claimed invention using the application, as filed, as a guide. MPEP 2164.05. The evidence need not be conclusive but merely convincing to one skilled in the art. Id. The evidence submitted must be reasonably related to the scope of the invention claimed.

The Examiner admits that the specification is enabled for a composition/ method comprising an ethanol or water extract of *Withania sominifera*. Claims

16 and 20 therefore have been amended to more specifically claim alcohol and/or aqueous extracts of *W. somnifera* Dunal. Applicants further direct the Examiner's attention to new claims 31-37, which depend directly or indirectly from claim 16, and new claims 38-44 which depend directly or indirectly from claim 20. Applicants further direct the Examiner's attention to new method claim 45, which claims a method of restoring male reproductive function compromised by an endocrine disturbing chemical comprising administering an effective amount of an alcohol and/or aqueous extract of a root, leaf or whole plant of *Withania somnifera* Dunal to a male subject in need of such treatment, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides.

In each of these claims, the extract has been defined to contain not less than 1 wt % of alkaloids and not less than 1 wt % withanolides. Example 1 in the specification provides a working example for obtaining the extract of the invention. Further support for these claims may be found in the specification on page 5, para. 1. As for the effective amount of the extract, the specification shows that, for example, the daily amount per adult human is generally in the range of 0.1 -10g. In addition, in Test Examples 1 and 2, experiments are carried out with 100 mg/kg or 500 mg/kg of *W. somnifera* extracts.

As for the effectiveness of *W. somnifera* extracts for restoring reproductive function, test examples 1-3 show the effectiveness of *W. somnifera* extracts with regard to reproduction. The Examiner has admitted that Table 6 displays data which indicates that rats treated with *W. somnifera* after ethynylestradiol administration displayed an increased sperm count as compared to the group which only received the gum arabic control. While the Examiner alleged that the data presented in the application concerning motility rates was unconvincing because there was no significant difference between treated and controls, motile sperm rate is not an important parameter, partly because the rate could increase occasionally even if the sperm count is less.

The Examiner further alleged that any claims as to the viability and reproductive nature of the sperm is highly questionable based on data in Garg. The Examiner's comparison based on Garg is inappropriate. First, Garg teaches that mice fed 25 mg doses of *W. sominifera* root powder show improved mating behavior, decreased litter size and infertility. However, no extract of the root was prepared. In the present invention, rats were treated with 100 mg/kg of a *W. sominifera* extract. The root extract prepared as described in the present disclosure is a product with unique pharmacological properties based upon its phytochemical constituents. See Revilla, et al., J. Agric. Food Chem. 46: 4592-97 (1998). The *W. sominifera* root powder in Garg is a different composition with different pharmacological properties. Therefore, it is inappropriate to compare the data in Garg to that disclosed herein. Second, Garg relates to experiments with normal animals. In contrast, the present invention targets male animals whose reproductive function has compromised by an endocrine disturbing chemical.

Applicants therefore urge that the effectiveness of *W. sominifera* extracts with regard to restoring compromised reproductive function is neither questionable nor unpredictable. Since a skilled artisan would not require undue experimentation to make and use the present invention, the specification meets the enablement requirement.

The Examiner further admits that the specification is enabled for a composition/method comprising an ethanol or water extract of *Withania sominifera* for increasing sperm count. Claims amended to claim a composition or method for restoring sperm count compromised by an endocrine disturbing chemical therefore would be enabled. Applicants direct the Examiner's attention to new claims 34-37 which claim a composition for restoring compromised reproductive function comprising an alcohol and/or aqueous extract of *Withania somnifera* Dunal wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, and wherein the reproductive function is

sperm count in a male subject. Likewise, Applicants direct the Examiner's attention to new claims 41-44 which claim a food supplement for restoring compromised reproductive function comprising a food and an alcohol and/or aqueous extract of Withania somnifera Dunal wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, and wherein the reproductive function is sperm count in a male subject. Further, Applicants direct the Examiner's attention to new claim 46 which claims a method of restoring male reproductive function compromised by an endocrine disturbing chemical comprising administering an effective amount of an alcohol and/or aqueous extract of a root, leaf or whole plant of Withania somnifera Dunal to a male subject in need of such treatment, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, and wherein the male reproductive function is sperm count of a male subject.

35 U.S.C. §102 Rejections

The Examiner alleged that Claims 16, 18, 20, 21, 29 and 30 are anticipated under 35 U.S.C. §102(a) by the article by Abdel-Mageid et al., J. Ethnopharmacology 75: 1-4 (2001) and that the composition was well known in the art. Abdel-Magied allegedly teaches that aqueous extracts from *W. somnifera*, administered as an aqueous solution to the stomach via a feeding tube, increase sperm count.

Applicants have amended the specification to make a claim for the benefit of an earlier filing date under 35 U.S.C. §119. The present invention met the requirements of 35 U.S.C. §371 on November 9, 2001, and claims priority to PCT International Application PCT/JP00/02940 filed May 9, 2000, which in turn claims the benefit of an international filing in Japan on May 10, 1999. Thus the Abdel-Magied reference is not prior art because the earliest filing date of the present application is before the 2001 date of publication of Abdel-Magied. Moreover, Abdel-Magied does not disclose or suggest that the extract of *W. somnifera* is effective in restoring male reproductive function compromised by an endocrine

disturbing chemical according to the present invention. Applicants therefore request that the Examiner withdraw this rejection.

The Examiner further alleged that claims 16, 18, 20 and 21 are anticipated under 35 U.S.C. §102(b) by U.S. Patent 5,83,698 to Chavali et al., and claim 16 by the abstract of Rao, et al. Indian J. Pharmaceutical Sciences 40(6): 236-37 (1978). Chavali allegedly describes a procedure for the aqueous extraction of *W. sominifera* roots to produce a pharmaceutical composition which was then filled into gel capsules, which would have been consumed (col. 4, lines 47-59). Rao allegedly teaches ether and ethanol extracts of *W. sominifera*.

Anticipation requires that each and every element of the claims be disclosed, either expressly or inherently, in a single prior art reference or embodied in a single prior art device or practice. MPEP 706.02 and 2131. There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. See Scripps Clinic & Res. Found. v. Genentech, Inc., 927 F.2d 1565, 1576, 18 U.S.P.Q.2d 1001 (Fed. Cir. 1991). Although absence of any claimed element from the reference negates anticipation (see Kloster Speedsteel AB v. Crucible, Inc., 793 F.2d 1565, 1571, 230 U.S.P.Q. 81 (Fed. Cir. 1986)), an unclaimed difference will not avoid anticipation. See SSIH Equip. S.A. v. United States ITC, 718 F.2d 365, 377, 218 U.S.P.Q. 678 (Fed. Cir. 1983). The discovery of a previously unknown property or use will not permit the patenting of an old product. See Harris Corp. v. IXYS Corp., 114 F.3d 1149, 1152, 43 U.S.P.Q.2d 1018 (Fed. Cir. 1997).

Applicants urge that the claims of the instant application are patentably distinguishable from the cited prior art. Neither of the references cited by the Examiner discloses or suggests that an extract of *W. sominifera* is effective in restoring male reproductive function compromised by an endocrine disturbing chemical.

First, the Examiner's interpretation of Rao is incorrect. Rao teaches that a powdered form of *W. sominifera* was administered orally and ethanol and ether extracts of *W. sominifera* roots were administered intraperitoneally to male rats. *W. sominifera* at 800 mg/kg produced a decrease in the sexual behavior of male rats (including homosexual mounting, sniffing, lying over one another, etc.). Since Rao does not disclose a composition for restoring compromised reproductive function comprising alcohol and/or aqueous extracts of *Withania sominifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, it does not anticipate amended claim 16 or new composition claims 31-33. Since Rao does not disclose a composition for restoring compromised reproductive function comprising alcohol and/or aqueous extracts of *Withania sominifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, and wherein the reproductive function is sperm count in a male subject, it does not anticipate new composition claims 34-37.

Furthermore, for Rao to be applied as a written publication under 35 U.S.C. §102(b), it must meet the disclosure requirements of 35 U.S.C. §112 para. 1. Each of the *W. sominifera* extracts disclosed in Rao is a different product with unique pharmacological properties based upon its phytochemical constituents. See Revilla, et al., *J. Agric. Food Chem.* 46: 4592-97 (1998). Each extract in turn is a different product from the *W. sominifera* powder disclosed in Rao. Rao does not teach or disclose which of these different products produced the observed result. Therefore, Rao's disclosure is insufficient to allow a skilled artisan to make and use the any of the products disclosed. Therefore, Rao, does not satisfy 35 U.S.C. §112 para. 1.

The Examiner's interpretation of the Chavalli reference also is incorrect. Claim 1 of the Chavalli reference requires that compositions contain an extract prepared from six varieties of herbs, each present in a physiologically acceptable amount. The specification teaches the advantages of that combination: it

describes a formulation comprising an herbal aqueous extract prepared from a combination of species of *Alpinia*, *Smilax*, *Tinospora*, *Tribulus*, *Withania* and *Zingiber* and its use, alone or as an ingredient in foods and beverages, to reduce and alleviate symptoms associated with rheumatoid arthritis, osteoarthritis, and reactive arthritis, and for reducing the production of proinflammatory cytokines. The term "extract" is defined as a concentrate of aqueous soluble plant components from the portion of the plant extracted and can be in aqueous or powdered form. The extracts from each herb are admixed together in physiologically acceptable amounts.

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Since Chavali does not disclose a composition for restoring compromised reproductive function comprising an alcohol or aqueous extract of *Withania somnifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, it does not anticipate amended claim 16 or new claims 31-33, which depend from amended claim 16. Further, since Chavali does not disclose a composition for restoring compromised reproductive function comprising an alcohol or aqueous extract of *Withania somnifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, and wherein the reproductive function is sperm count in a male subject, it does not anticipate new claims 34-37. Further, since Chavali does not disclose a food supplement for restoring compromised reproductive function comprising a food and an alcohol or aqueous extract of *Withania somnifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, it does not anticipate amended claim 20 or new claims 38-40 which depend from claim 20. Further, since Chavali does not disclose a food supplement for restoring compromised reproductive function comprising an alcohol or aqueous extract of *Withania somnifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides, and wherein the reproductive function is sperm count in a male subject, it does not anticipate new claims 41-44.

Applicant earnestly solicits early and favorable action by the Examiner on this application. If the Examiner believes that issues may be resolved by a telephone interview, the Examiner is respectfully urged to telephone the undersigned at 212-801-2146. The undersigned may also be contacted via e-mail at rzucidloe@gtlaw.com.

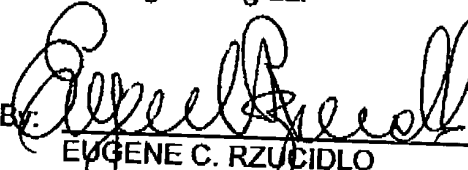
AUTHORIZATION

The Commissioner is hereby authorized to charge any fees which may be required, or credit any overpayment to Deposit Account No. 50-1561.

Respectfully submitted,

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Date: December 10, 2002

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Amendment

16. (Amended) A composition for restoring compromised reproductive function comprising an aqueous and/or alcohol extract of *Withania somnifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides.
20. (Amended) A food supplement for restoring compromised reproductive function comprising a food and an aqueous and/or alcohol extract of *Withania somnifera* Dunal, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides.
31. (New) The composition of claim 16, wherein the extract is an aqueous extract.
32. (New) The composition of claim 16, wherein the extract is an alcohol extract.
33. (New) The composition of claim 32, wherein the alcohol is ethanol.
34. (New) The composition of claim 16, wherein the reproductive function is sperm count in a male subject.
35. (New) The composition of claim 34, wherein the extract is an aqueous extract.
36. (New) The composition of claim 34, wherein the extract is an alcohol extract.
37. (New) The composition of claim 36, wherein the alcohol is ethanol.
38. (New) The food supplement of claim 20, wherein the extract is an aqueous extract.
39. (New) The food supplement of claim 20, wherein the extract is an alcohol extract.
40. (New) The food supplement of claim 39, wherein the alcohol is ethanol.

41. (New) The composition of claim 20, wherein the reproductive function is sperm count in a male subject.
42. The food supplement of claim 41, wherein the extract is an aqueous extract.
43. The food supplement of claim 41, wherein the extract is an alcohol extract.
44. The food supplement of claim 43, wherein the alcohol is ethanol.
45. (New) A method of restoring male reproductive function compromised by an endocrine disturbing chemical comprising administering an effective amount of an alcohol and/or aqueous extract of a root, leaf or whole plant of Withania somnifera Dunal to a male subject in need of such treatment, wherein the extract contains not less than 1 wt % of alkaloids and not less than 1 wt % withanolides.
46. (New) The method of claim 45, wherein the male reproductive function is sperm count of a male subject.